



OPA1 gene

OPA1, mitochondrial dynamin like GTPase

Normal Function

The *OPA1* gene provides instructions for making a protein that helps determine the shape and structure (morphology) of mitochondria, the energy-producing centers within cells. The *OPA1* protein is made in many types of cells and tissues, including the brain, the light-sensitive tissue at the back of the eye (the retina), muscles used for movement (skeletal muscles), the liver, and the heart. Within cells, this protein is found in the inner membrane of mitochondria. Mitochondria are dynamic structures that undergo changes in morphology through processes called fission (splitting into smaller pieces) and fusion (combining pieces). These changes in morphology are necessary for mitochondria to function properly. The *OPA1* protein helps to regulate the morphology of mitochondria by playing a key role in the fusion process.

The *OPA1* protein is also involved in a process called oxidative phosphorylation, from which cells derive much of their energy. Additionally, the *OPA1* protein plays a role in the maintenance of the small amount of DNA within mitochondria, called mitochondrial DNA (mtDNA), and in the self-destruction of cells (apoptosis).

Health Conditions Related to Genetic Changes

optic atrophy type 1

More than 200 mutations in the *OPA1* gene have been found to cause optic atrophy type 1. Most of these mutations create a premature stop signal in the instructions for making the *OPA1* protein. As a result, an abnormally small protein is produced, which is likely to be unstable and broken down quickly. The most common mutation that causes optic atrophy type 1 deletes four DNA building blocks (nucleotides) in the *OPA1* gene (written as 2708delTTAG).

OPA1 gene mutations lead to overall dysfunction of the mitochondria and the breakdown of structures that transmit visual information from the eyes to the brain. Affected individuals first experience a progressive loss of nerve cells that line the retina, called retinal ganglion cells. The loss of these cells is followed by the degeneration (atrophy) of the optic nerve. The optic nerve is partly made up of specialized extensions of retinal ganglion cells called axons; when the retinal ganglion cells die, the optic nerve cannot transmit visual information to the brain normally. It is unclear why the *OPA1* gene mutations that cause optic atrophy type 1 only affect the eyes. Retinal ganglion cells have many mitochondria and especially

high energy requirements, which researchers believe may make them particularly vulnerable to mitochondrial dysfunction and decreases in energy production.

progressive external ophthalmoplegia

other disorders

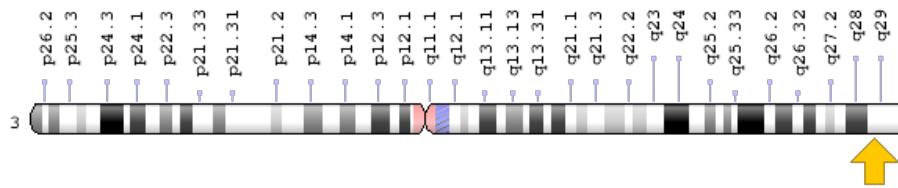
Some mutations in the *OPA1* gene cause the features of optic atrophy type 1 but also affect other body systems. One condition, called optic atrophy type 1 and deafness, causes vision loss and hearing loss. *OPA1* mutations also cause a second, more severe condition known as autosomal dominant optic atrophy (ADOA)-plus syndrome. This condition involves vision loss, weakness in the muscles that control eye movement (progressive external ophthalmoplegia), difficulty with balance and coordination (ataxia), hearing loss, disturbances in the nerves used for muscle movement and sensation (motor and sensory neuropathy), and muscle weakness (myopathy).

In most cases, these two conditions are caused by the same mutation. This mutation replaces the protein building block (amino acid) arginine with the amino acid histidine at position 445 in the *OPA1* protein (written as Arg445His or R445H). It is unclear why the R445H mutation causes other features in addition to vision loss in affected individuals.

Chromosomal Location

Cytogenetic Location: 3q29, which is the long (q) arm of chromosome 3 at position 29

Molecular Location: base pairs 193,593,144 to 193,697,811 on chromosome 3 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- FLJ12460
- KIAA0567
- MGM1

- mitochondrial dynamin-like GTPase
- NPG
- NTG
- OPA1_HUMAN
- optic atrophy 1 (autosomal dominant)

Additional Information & Resources

Educational Resources

- Neuroscience (second edition, 2001): Central Projections of Retinal Ganglion Cells
<https://www.ncbi.nlm.nih.gov/books/NBK11145/>
- Neuroscience (second edition, 2001): Central Projections of Retinal Ganglion Cells (picture)
<https://www.ncbi.nlm.nih.gov/books/NBK11145/figure/A825/>
- Webvision--The Organization of the Retina and Visual System: Retinal Ganglion Cells
https://www.ncbi.nlm.nih.gov/books/NBK11558/#ch20wong.Retinal_Ganglion_Cel

GeneReviews

- Optic Atrophy Type 1
<https://www.ncbi.nlm.nih.gov/books/NBK1248>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28OPA1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>

OMIM

- OPA1 GENE
<http://omim.org/entry/605290>
- OPTIC ATROPHY WITH OR WITHOUT DEAFNESS, OPHTHALMOPLEGIA, MYOPATHY, ATAXIA, AND NEUROPATHY
<http://omim.org/entry/125250>

Research Resources

- **Atlas of Genetics and Cytogenetics in Oncology and Haematology**
http://atlasgeneticsoncology.org/Genes/GC_OPA1.html
- **ClinVar**
<https://www.ncbi.nlm.nih.gov/clinvar?term=OPA1%5Bgene%5D>
- **HGNC Gene Symbol Report**
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=8140
- **NCBI Gene**
<https://www.ncbi.nlm.nih.gov/gene/4976>
- **UniProt**
<http://www.uniprot.org/uniprot/O60313>

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